AMENDMENTS TO THE CLAIMS

Upon filing this divisional application, the accompanying Request cancels claims 1-52 from the parent application. The present document further cancels claims 64 and 65, amends claims 53-58, 61-63 and 66-75 and adds claims 76-97. According to 37 C.F.R. § 1.121(c), after entry of the present amendment, the status of the claims in the case is as follows:

Claims 1-52 cancelled

53. (Currently Amended) A liquid-crystalline multimolecular aggregate comprising a plurality of amphiphilic molecules dispersed in an aqueous solution, said amphiphilic molecules ~~each comprising a hydrophilic compound having attached, at spatially distinct sites, at least two hydrophobic moieties~~ comprising a hydrophilic component having at least a first and second terminus and at least a first and second hydrophobic moiety separately attached to, or proximal to, said first and second terminus of said hydrophilic component.

54. (Currently Amended) A liposome or lipid complex comprising ~~an~~ amphiphilic ~~molecule~~ molecules that ~~comprises~~ comprise a hydrophilic ~~compound~~ component positioned over at least a portion of the outer surface of said liposome or lipid complex~~, the hydrophilic compound having attached, at spatially distinct sites, at least two hydrophobic moieties that extend into the hydrophobic bilayer of said liposome or lipid complex~~; wherein said hydrophilic component has at least a first and second terminus and at least a first and second hydrophobic moiety separately attached to, or proximal to, said first and second terminus, wherein said first and second hydrophobic moieties extend into the hydrophobic bilayer of said liposome or lipid complex.

55. (Currently Amended) The liposome or lipid complex of claim 54, wherein said amphiphilic ~~molecule comprises~~ molecules comprise a plurality of hydrophobic moieties that extend into the hydrophobic bilayer of said liposome or lipid complex and wherein said hydrophilic ~~compound~~ component is positioned over a substantial portion of the outer surface of said liposome or lipid complex.

56. (Currently Amended) ~~A~~ The method of ~~making an amphiphilic molecule, comprising attaching at least two hydrophobic moieties to spatially distinct sites of a hydrophilic compound~~ claim 57, wherein said amphiphilic molecules are prehydrated amphiphilic molecules.

57. (Currently Amended) A method of making a liposome or lipid complex comprising admixing, in an excess of an aqueous solution, a population of lipid components with a population of ~~prehydrated amphiphilic molecules that comprise a hydrophilic compound having at least two hydrophobic moieties attached at spatially distinct sites, said admixing effective to form a liposome or lipid complex~~ amphiphilic molecules; wherein said amphiphilic molecules comprise a hydrophilic component having at least a first and second terminus and at least a first and second hydrophobic moiety separately attached to, or proximal to, said first and second terminus; and wherein said admixing is effective to form said liposome or lipid complex.

58. (Currently Amended) A method of making an amphiphilic material-coated liposome, lipid complex or biological cell, comprising:

(a) providing a liposome, lipid complex or biological cell; and

(b) contacting ~~a~~ said liposome, lipid complex or biological cell with an amphiphilic material that comprises a hydrophilic ~~compound having at least two hydrophobic moieties attached at spatially distinct sites, such that said~~ component having at least a first and second terminus and at least a first and second hydrophobic moiety separately attached to, or proximal to, said first and second terminus; wherein said first and second hydrophobic moieties extend into the hydrophobic bilayer of said liposome, lipid complex or cell and wherein said hydrophilic ~~compound~~ component is positioned over at least a portion of the surface of said liposome, lipid complex or cell;

thereby forming an amphiphilic material-coated liposome, lipid complex or biological cell.

59. (Original) The method of claim 58, wherein said biological cell is a red blood cell.

60. (Original) The method of claim 59, wherein said biological cell is a human red blood cell.

61. (Currently Amended) ~~A~~ The method of claim 57, further comprising admixing ~~encapsulating or entrapping a selected agent in a~~ said liposome or lipid complex~~, comprising admixing~~ with a selected agent ~~with a population of liposomes or lipid complexes that comprise an amphiphilic molecule that comprises a hydrophilic compound positioned over at least a portion of the outer surface of the liposome or complex, the hydrophilic compound having attached, at spatially distinct sites, at least two hydrophobic moieties that extend into the~~

~~hydrophobic bilayer of the liposome or complex~~, wherein said admixing is effective to cause encapsulation or entrapment of said selected agent in said liposome or lipid complex.

62. (Currently Amended) A kit comprising, in a suitable container ~~means~~, ~~an~~ amphiphilic ~~molecule~~ molecules comprising a hydrophilic ~~compound having attached, at spatially distinct sites, at least two hydrophobic moieties~~ component having at least a first and second terminus and at least a first and second hydrophobic moiety separately attached to, or proximal to, said first and second terminus; or a liposomal formulation comprising said amphiphilic molecule.

63. (Currently Amended) The ~~kit~~ method of claim ~~62~~ 61, wherein said ~~kit further comprises a~~ selected agent is a blood product.

Claims 64 and 65 cancelled

66. (Currently Amended) ~~A~~ The method ~~for providing a~~ of claim 61, wherein said selected agent ~~to an animal, comprising administering to said animal a medicinal delivery composition comprising, in a pharmaceutically acceptable vehicle, a population of liposomes or lipid complexes comprising said selected agent; wherein said liposomes or complexes comprise an amphiphilic molecule that comprises a hydrophilic compound positioned over at least a portion of the outer surface of the liposome or complex, the hydrophilic compound having attached, at spatially distinct sites, at least two hydrophobic moieties that extend into the hydrophobic bilayer of the liposome or lipid complex~~ is an immunological component.

67. (Currently Amended) The method of claim ~~66~~ 61, wherein said selected agent is a nutrient or a nutritional supplement.

68. (Currently Amended) The method of claim ~~66~~ 63, wherein said selected agent is an oxygen carrier, haemoglobin~~,~~ or a coagulant ~~or a blood product~~.

69. (Currently Amended) The method of claim 66, wherein said selected agent is an antigen, an antibody, ~~an immunological component,~~ a cytokine or an anti-inflammatory agent.

70. (Currently Amended) The method of claim ~~66~~ 61, wherein said selected agent is a chemotherapeutic agent or cytotoxin.

71. (Currently Amended) The method of claim ~~66~~ 61, wherein said selected agent is ~~an~~ a protein, peptide, enzyme, hormone, growth factor or neurotransmitter.

72. (Currently Amended) The method of claim ~~66~~ 61, wherein said selected agent is an antibiotic, an anti-viral or a fungicide.

73. (Currently Amended) The method of claim ~~66~~ 61, wherein said selected agent is an anaesthetic or a surfactant.

74. (Currently Amended) The method of claim ~~66~~ 61, wherein said selected agent is ~~a nucleic acid molecule,~~ nucleic acid molecules, a nucleic acid construct or vector, an antisense nucleic acid or a ribozyme.

75. (Currently Amended) The method of claim ~~66~~ 61, wherein said ~~animal is a human subject~~ selected agent is an agent from Table 3A, Table 3B or Table 4.

76. (New) The method of claim 61, wherein said selected agent is a pheromone or an agricultural agent.

77. (New) The method of claim 57, wherein said hydrophilic component of said amphiphilic molecules is a substantially linear, a branched, a pendant or a star hydrophilic component.

78. (New) The method of claim 57, wherein said hydrophilic component of said amphiphilic molecules is a hydrophilic component from Table 1.

79. (New) The method of claim 57, wherein at least one of said hydrophobic moieties of said amphiphilic molecules is a hydrophobic moiety from Table 2.

80. (New) The method of claim 79, wherein at least one of said hydrophobic moieties of said amphiphilic molecules is a deoxy-amino, deoxy-N-methylamino, deoxy-N,N dimethylamino, deoxy-N,N-dimethyl-N-alkylammonium or deoxy-N,N,N trialkylammonium analogue of a glyceride, wherein said glyceride is a glycerol fattyacid ester/ether, a monoglyceride (mono-

fattyacylglycerol), monoalkylglycerol, diglyceride (difattyacylglycerol) or monoalkyl-monofattyacylglycerol.

81. (New) The method of claim 57, wherein said amphiphilic molecules are bipodal amphiphilic molecules comprising a substantially linear hydrophilic component that has a first and second terminus, and wherein a first and second hydrophobic moiety are separately attached at, or substantially at, said first and second terminus.

82. (New) The method of claim 57, wherein said amphiphilic molecules are oligopodal or polypodal amphiphilic molecules comprising a branched or star hydrophilic component that has a plurality of termini and a plurality of hydrophobic moieties separately attached to each terminus or proximal thereto.

83. (New) The method of claim 82, wherein said amphiphilic molecules comprise a plurality of hydrophobic moieties that extend into the hydrophobic bilayer of said liposome or lipid complex and wherein said hydrophilic component is positioned over a substantial portion of the outer surface of said liposome or lipid complex.

84. (New) The method of claim 57, wherein said liposome or lipid complex comprises between 1% and 99% of said amphiphilic molecules.

85. (New) The method of claim 57, wherein said liposome or lipid complex comprises about 100% of said amphiphilic molecules.

86. (New) The method of claim 57, wherein said amphiphilic molecules are non-ionic species.

87. (New) The method of claim 57, wherein said amphiphilic molecules are charge neutral zwitterionic species.

88. (New) The method of claim 57, wherein said amphiphilic molecules are (poly)anionic species.

89. (New) The method of claim 57, wherein said amphiphilic molecules are (poly)cationic species.

90. (New) The method of claim 57, wherein said amphiphilic molecules comprise branching points or functional groups.

91. (New) The method of claim 90, wherein said branching points or functional groups are provided by glycerol, pentaerythritol, polyols, hydroxy, amino acids or peptides.

92. (New) The method of claim 90, wherein said branching points or functional groups are attached to lipid residues.

93. (New) The method of claim 92, wherein said branching points or functional groups are attached to said lipid residues via linkers or spacer residues.

94. (New) The method of claim 90, wherein said branching points or functional groups are attached to antigens, antibodies or pendant ligands.

95. (New) The method of claim 94, wherein said branching points or functional groups are attached to fluorescent, spin, biotin or thio-gold labels or to chelators.

96. (New) The method of claim 94, wherein said branching points or functional groups are attached to antigens, antibodies or pendant ligands via linkers or spacer residues.

97. (New) A method of encapsulating or entrapping a selected agent in a liposome or lipid complex, comprising:

(a) providing a population of liposomes or lipid complexes that comprise amphiphilic molecules that comprise a hydrophilic component positioned over at least a portion of the outer surface of the liposome or lipid complex; wherein said hydrophilic component has at least a first and second terminus and at least a first and second hydrophobic moiety separately attached to, or proximal to, said first and second terminus, wherein said first and second hydrophobic moieties extend into the hydrophobic bilayer of the liposome or lipid complex; and

(b) admixing said selected agent with said population of liposomes or lipid complexes, wherein said admixing is effective to cause encapsulation or entrapment of said selected agent in said liposome or lipid complex.

REMARKS

I. Divisional Application Status

The present application is a divisional of allowed, co-pending application Serial No. 09/879,368, filed June 11, 2001 ("the '368 application"; Attorney Docket Nos. 4020.000282; NUBI:002--1). The '368 application is a divisional of application Serial No. 08/912,978, filed August 13, 1997 ("the '978 application"; Attorney Docket Nos. 4020.000200; NUBI:002). The inventorship remains the same as the earlier applications.

The '978 application was filed with claims 1-75, which were restricted into two patentably distinct inventions. The Group I invention was first elected and the claims issued.

The '368 application was filed as a divisional of the '978 application, directed to the Group II invention. Despite begin directed to the single, Group II invention, the original claims in the '368 application were initially restricted into five allegedly patentably distinct inventions. The Office separated the methods of making (Groups II and III) from the compositions and methods of using (Groups I, IV and V). The Office later agreed that Groups IV and V were drawn to a single invention, which was elected, allowed and will issue.

The present application is a divisional of the '368 application, mainly drawn to the methods of making (claims 57-61). The Office earlier placed claims 57-60 in the Group II invention and claim 61 alone in the Group III invention. Presently, claim 61 is being amended to depend from claim 57, thus clearly establishing unity for the methods of making.

As the five-way restriction requirement in the '368 application was at odds with the two-way restriction requirement in the '978 application, Applicant is including claims 53-55 and 62 in the present application. These claims reflect the Group I invention from the '368 application.

Applicant respectfully requests that the preceding amendments to the specification and claims be entered prior to substantive examination of this application. All of the amendments and additionally presented claims are fully supported by the parent and provisional applications, to which priority is still properly claimed.

II. Status of the Claims

Claims 1-52, 64 and 65 from the parent application have been canceled. Claims 53-58, 61-63 and 66-75 have been amended. Claims 76-97 have been added, which are fully supported by the application as filed and are unified with the method of making claims.

Claims 53-63 and 66-97 are therefore in the case.

III. Compliance with 37 C.F.R. § 1.121

The claim for priority has been timely introduced into the specification by amendment of the opening paragraph at page 2. The amendment to the specification complies with 37 C.F.R. § 1.121. According to the current 37 C.F.R. § 1.121(c), a copy of the pending claims is provided in the amendment section.

IV. The Claims are Allowable

The original grandparent, '978 application has issued. The parent, '368 application has been allowed and claims will issue to the unified invention of Groups IV and V.

The present claims are mainly directed to methods of making the compositions allowed in the parent application. The amphiphilic molecules, liposomes, lipid complexes and selected agents of the present claims are defined using the same language as allowed in the parent and grandparent applications.

The substantive correspondence between the issued and allowed claims and those of the present application compels a finding of patentability for this divisional application. Given that all requirements of patentability have been addressed in the parent and grandparent applications, leading to allowance and issuance, the presently claimed invention should also be free from rejection. Applicant therefore urges that the present claims be immediately progressed to allowance.

V. Additional Support for the Claims

Claims 53-55 and 57 are original claims, clarified at certain points with the language of the issued and allowed claims in the grandparent and parent applications. Additional support for these claims exists in original claims 40, 44 and 54.

Claim 56 has been revised to further define the amphiphilic molecules of claim 57 as prehydrated amphiphilic molecules, which is supported throughout the specification, *e.g.*, at least at page 22, lines 12-24.

Claim 58 incorporates the language of the issued and allowed claims in the grandparent and parent applications, and has further support in original claim 50. For ease of review, this claim is now presented in the (a) and (b) format. The body of the claim is also even more clearly linked to the preamble by use of the "thereby" clause.

Claim 61 has been amended to depend from claim 57.

Claim 62 has been revised to match the language of the issued and allowed claims in the grandparent and parent applications.

Claim 63 has been amended to further define the selected agent of the claimed methods as a blood product, as supported by original claim 68.

Claim 66 has been revised to further define the selected agent of the claimed methods as an immunological component, as supported by original claim 69.

In claim 67, the term "nutrient" has been added to nutritional supplement. In claim 68, the term "oxygen carrier" has been added to haemoglobin and coagulant. Each of the additional terms are supported by allowed claim 48 in the '978 application.

In claim 71, the terms "protein and peptide" are included with enzyme, hormone, growth factor and neurotransmitters, as supported throughout the original application, *e.g.*, at least at page 3, line 17 and at page 49, line 4.

In claim 74, "antisense nucleic acid and ribozyme" has been added to the listed nucleic acid molecules, as supported by allowed claim 48 in the '978 application.

Claims 75, 78 and 79 are clearly supported by Tables 3A, 3B and 4 (claim 75) and Tables 1 and 2 (claims 78 and 79) of the specification.

New claim 76 identifies the selected agent as a pheromone or an agricultural agent, as supported by the specification and in claim 48 in the patent issued from the '978 application.

New claim 77 is based upon allowed claim 4 from the '978 application.

Dependent claim 80 further defines the hydrophobic moieties as particular examples from Table 2, which provides the required support.

Claims 81, 82 and 83 are supported by allowed claims 25, 27-28 and 45 in the '978 application, respectively.

New claims 84 and 85 define the % of the amphiphilic molecules in the liposomes or lipid complexes, which are supported throughout the original application, *e.g.*, at least from page 19, line 20 to page 20, line 2.

Claims 86, 87, 88 and 89 define the amphiphilic molecules of the claimed methods as being non-ionic, charge neutral zwitterionic, (poly)anionic and (poly)cationic species, respectively. These claims have support throughout the original application, *e.g.*, at least at page 36, lines 22-26.

New claims 90-96 separately define the amphiphilic molecules as comprising branching points or functional groups (claims 90 and 91), optionally attached to lipid residues (claim 92) or functional groups such as antigens, antibodies or pendant ligands (claim 94), fluorescent, spin, biotin or thio-gold labels or to chelators (claim 95), via linkers or spacer residues (claims 93 and 96). These claims are supported throughout the original application, *e.g.*, at least at page 28, lines 20-25 and in FIG. 7 and FIG. 8 and the description thereof at page 25, lines 18-24.

Finally, new claim 97 is based on independent claim 61 prior to amendment.

It will therefore be understood that no new matter is included within any of the claims submitted as part of the present application.

VI. Formalities

The proper claim for priority is introduced into the specification by amendment. Formal drawings are enclosed herewith. Applicant's initial duty of disclosure is also met.

Should the Office require a Terminal Disclaimer to secure allowance, Applicant respectfully solicits a telephone call to the Applicant's representative so that the matter can be addressed without delay.

No fees should be due in addition to the enclosed filing fees. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Commissioner is authorized to deduct said fees from Williams, Morgan & Amerson, P.C. Deposit Account No. 50-0786/4020.000283.

VII. Conclusion

In conclusion, Applicant submits that, in light of the foregoing remarks, the present claims are in condition for allowance and an early indication to this effect is respectfully requested. Should the examiner have any questions or comments, a telephone call to the undersigned Applicant's representative is earnestly solicited.

Respectfully submitted,
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